PHREND©: External validation of model to predict individual efficacy of disease modifying therapies (DMT) in relapsing-remitting multiple sclerosis (RRMS)

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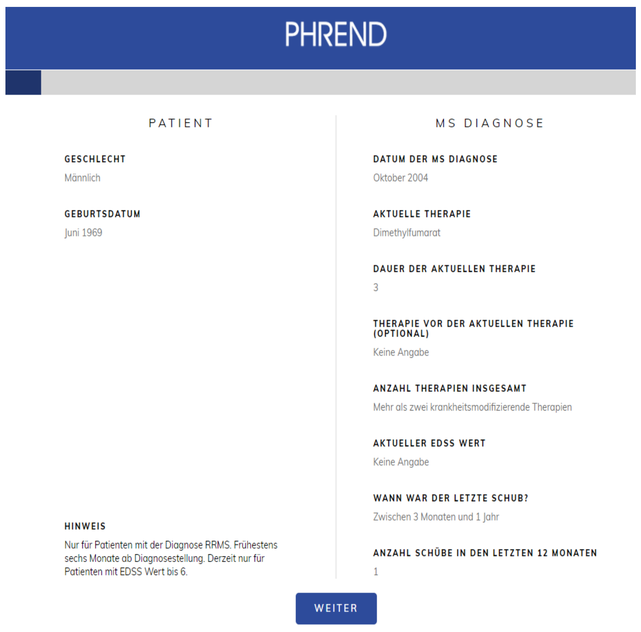
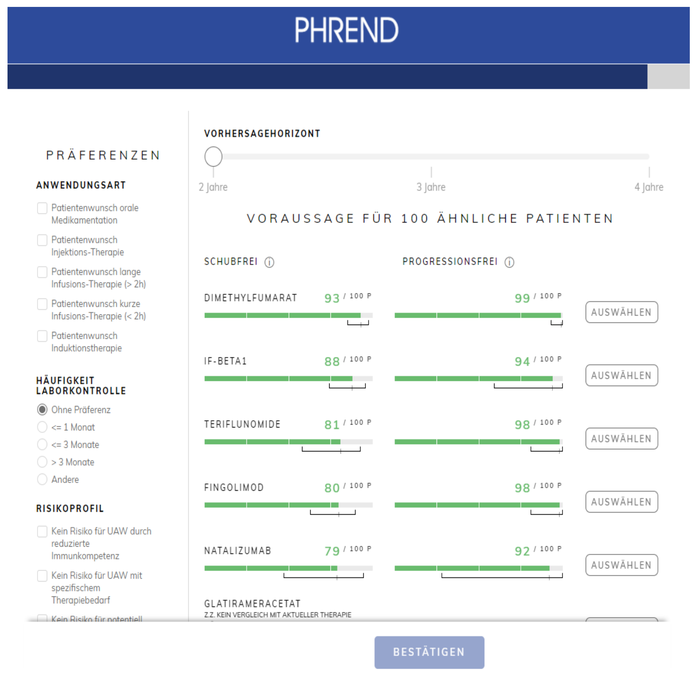
Background:



Based on real-world data of the NeuroTransData (NTD) MS registry a mathematical model was developed based on generalized linear models and Bayesian inference, which calculates the individual probabilities to achieve freedom of relapse activity and of 3-month-confirmed-EDSS-progression (3mCEP) for a single patient predictively from 2 to 4 years for almost all DMTs available. Results of Internal validation showing good results for discrimination and accuracy have already been communicated. Here, the results of the external validation are shown.



Methods:

External cohort data: Published results of active treatment arms of the clinical trials CONFIRM (dimethylfumarate, glatirameracetate), DEFINE (dimethylfumarate), REGARD (interferon-ß, glatirameracetate), TRANSFORMS (interferon-ß, fingolimod).

Study	Year	DMTs	N	Authors	Notes
CONFIRM	2012	DMF, GA	350, 359	Fox, Miller, et al.	"Confirmed relapse"
DEFINE	2013	DMF	826	Bar-Or, Gold, et al.	"Confirmed relapse"
REGARD	2008	Rebif, GA	386, 378	Mikol, Barkhof, et al.	
TRANSFORMS	2011	FTY, IFN	849, 431	Cohen, Barkhof, et al.	"Confirmed relapse"

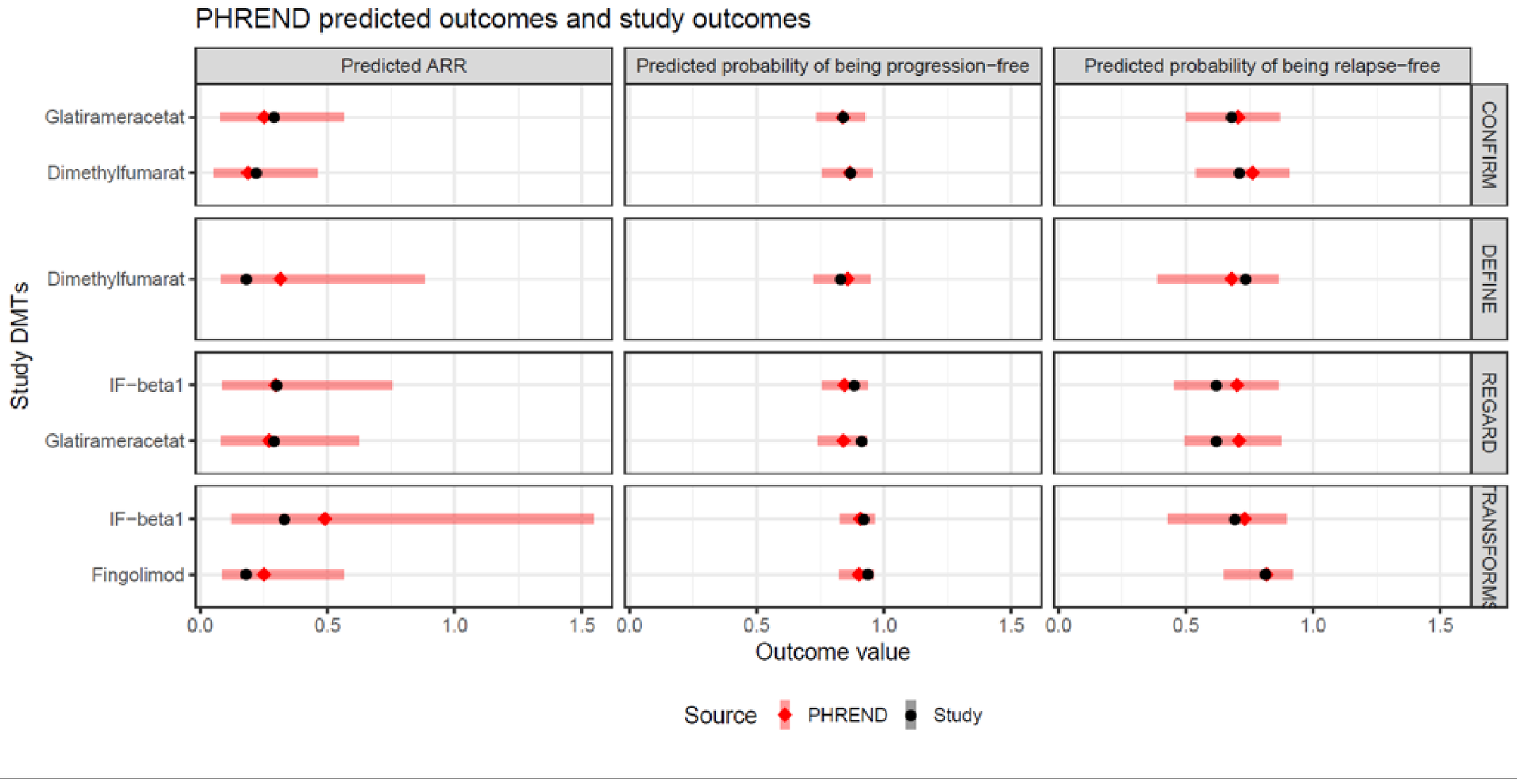
Statistical methods: For each study population a cohort in the NTD MS registry was identified with matching clinical and demographic characteristics. Annualized relapse rates and probabilities of the PHREND (Predictive Healthcare with Real-World Evidence for Neurological Disorders) algorithm to achieve freedom of relapse activity and 3mCEP were compared with study result.

Results:

There was a high consistency between the PHREND algorithm and the clinical study results for both outcome parameters. The predictive outcome probabilities of PHREND closely matched the results from 4 clinical studies and seven active treatments.

This positive validation of PHREND by external data further underlines validity and accuracy of this model. Additional validation projects are in progress.

Therapy	Endpoint	Study	Mean difference	Mean study	Mean phrend	Q05 phrend	Q95 phrend	N_study	N_phrend
Dimethylfumarat	Predicted ARR	CONFIRM	-0.03	0.22	0.19	0.05	0.46	350	159
Glatirameracetat	Predicted ARR	CONFIRM	-0.04	0.29	0.25	0.08	0.57	359	159
Dimethylfumarat	Predicted ARR	DEFINE	0.13	0.18	0.32	0.08	0.88	826	746
Glatirameracetat	Predicted ARR	REGARD	-0.02	0.29	0.27	0.08	0.62	378	147
IF-beta1	Predicted ARR	REGARD	0.00	0.30	0.30	0.09	0.76	386	147
Fingolimod	Predicted ARR	TRANSFORMS	0.07	0.18	0.25	0.09	0.56	849	671
IF-beta1	Predicted ARR	TRANSFORMS	0.16	0.33	0.49	0.12	1.55	431	671
Dimethylfumarat	Predicted probability of being progression-free	CONFIRM	0.00	0.87	0.87	0.76	0.95	350	159
Glatirameracetat	Predicted probability of being progression-free	CONFIRM	0.00	0.84	0.84	0.73	0.93	359	159
Dimethylfumarat	Predicted probability of being progression-free	DEFINE	0.03	0.83	0.86	0.72	0.95	826	746
Glatirameracetat	Predicted probability of being progression-free	REGARD	-0.07	0.91	0.84	0.74	0.93	378	147
IF-beta1	Predicted probability of being progression-free	REGARD	-0.04	0.88	0.85	0.76	0.94	386	147
Fingolimod	Predicted probability of being progression-free	TRANSFORMS	-0.04	0.94	0.90	0.82	0.96	849	671
IF-beta1	Predicted probability of being progression-free	TRANSFORMS	-0.01	0.92	0.91	0.83	0.96	431	671
Dimethylfumarat	Predicted probability of being relapse-free	CONFIRM	0.05	0.71	0.76	0.54	0.91	350	159
Glatirameracetat	Predicted probability of being relapse-free	CONFIRM	0.03	0.68	0.71	0.50	0.87	359	159
Dimethylfumarat	Predicted probability of being relapse-free	DEFINE	-0.05	0.74	0.68	0.39	0.87	826	746
Glatirameracetat	Predicted probability of being relapse-free	REGARD	0.09	0.62	0.71	0.50	0.88	378	147
IF-beta1	Predicted probability of being relapse-free	REGARD	0.08	0.62	0.70	0.45	0.87	386	147
Fingolimod	Predicted probability of being relapse-free	TRANSFORMS	0.00	0.81	0.82	0.65	0.92	849	671
IF-beta1	Predicted probability of being relapse-free	TRANSFORMS	0.04	0.69	0.73	0.43	0.89	431	671



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